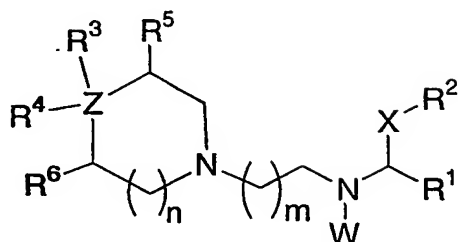


WHAT IS CLAIMED IS:

1. A compound of the formula I:



I

wherein:

X is selected from the group consisting of:

-NR¹⁰-, -O-, -CH₂O-, -CONR¹⁰-, -NR¹⁰CO-, -CO₂-, -OCO-,
-CH₂(NR¹⁰)CO-, -N(COR¹⁰)-, -CH₂N(COR¹⁰)-, phenyl, and

C₃₋₆ cycloalkyl,

where R¹⁰ is independently selected from: hydrogen, C₁₋₆ alkyl, benzyl, phenyl, and
C₁₋₆ alkyl-C₃₋₆ cycloalkyl,

which is unsubstituted or substituted with 1-3 substituents where the substituents
are independently selected from: halo, C₁₋₃alkyl,

C₁₋₃alkoxy and trifluoromethyl;

W is selected from:

hydrogen and C₁₋₆ alkyl, which is unsubstituted or substituted with 1-3
substituents where the substituents are independently selected from: halo, C₁₋₃-
alkoxy and trifluoromethyl;

Z is selected from:

C, N, and -O-, wherein when Z is N, then R⁴ is absent, and when W is -O-, then both R³
and R⁴ are absent;

n is an integer selected from 0, 1, 2, 3 and 4;

m is an integer selected from 1, 2, 3 and 4;

R¹ is selected from:

hydrogen, -C₀₋₆alkyl-, -(C₀₋₆alkyl)-alkenyl-,
-(C₀₋₆alkyl)-C₃₋₆cycloalkyl, -(C₀₋₆alkyl)-phenyl,
and -(C₀₋₆alkyl)-heterocycle,

where the alkyl is unsubstituted or substituted with 1-7 substituents where the substituents are independently selected from:

- (a) halo,
- (b) hydroxy,
- (c) -O-C₁₋₃alkyl,
- (d) trifluoromethyl, and
- (e) -C₁₋₃alkyl,

and where the phenyl and the heterocycle is unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from:

- (a) halo,
- (b) hydroxy; alkoxy
- (c) amino; acylamino; sulfonylamino; alkoxycarbonylamino
- (d) carboxylic acid; carbamide; sulfonamide

or wherein W and R¹ may be joined together to form a ring by a group selected from:

-(C₁₋₆alkyl)-, -C₀₋₆alkyl-Y-(C₁₋₆alkyl)-, and
-(C₀₋₆alkyl)-Y-(C₀₋₆alkyl)-(C₃₋₇cycloalkyl)-(C₀₋₆alkyl),

where Y is selected from:

a single bond, -O-, -S-, -SO-, -SO₂-, and -NR¹⁰-,

and where the alkyl and the cycloalkyl are unsubstituted or substituted with 1-7 substituents where the substituents are independently selected from:

- (a) halo,
- (b) hydroxy,
- (c) -O-C₁₋₃alkyl, and
- (d) trifluoromethyl,
- (e) C₁₋₃alkyl,
- (f) -O-C₁₋₃alkyl,
- (g) -CO₂R⁹, wherein R⁹ is independently selected from: hydrogen, C₁₋₆ alkyl, C₅₋₆ cycloalkyl, benzyl or phenyl, which is unsubstituted or

substituted with 1-3 substituents where the substituents are independently selected from: halo, C₁₋₃alkyl, C₁₋₃alkoxy and trifluoromethyl,

- (h) -CN,
- (i) -NR⁹R¹⁰,
- (j) -NR⁹COR¹⁰,
- (k) -NR⁹SO₂R¹⁰, and
- (l) -CONR⁹R¹⁰;

R² is selected from:

(C₀₋₆alkyl)-phenyl and (C₀₋₆alkyl)-heterocycle,

where the alkyl is unsubstituted or substituted with 1-7 substituents where the substituents are independently selected from:

- (a) halo,
- (b) hydroxy,
- (c) -O-C₁₋₃alkyl,
- (d) trifluoromethyl, and
- (e) -C₁₋₃alkyl,

and where the phenyl and the heterocycle is unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from:

- (a) halo,
- (b) trifluoromethyl,
- (c) trifluoromethoxy,
- (d) hydroxy,
- (e) C₁₋₆alkyl,
- (f) C₃₋₇cycloalkyl,
- (g) -O-C₁₋₆alkyl,
- (h) -O-C₃₋₇cycloalkyl,
- (i) -SCF₃,
- (j) -S-C₁₋₆alkyl,
- (k) -SO₂-C₁₋₆alkyl,
- (l) phenyl,
- (m) heterocycle,
- (n) -CO₂R⁹,
- (o) -CN,

- (p) $-\text{NR}^9\text{R}^{10}$,
- (q) $-\text{NR}^9-\text{SO}_2-\text{R}^{10}$,
- (r) $-\text{SO}_2-\text{NR}^9\text{R}^{10}$, and
- (s) $-\text{CONR}^9\text{R}^{10}$;

5

R^3 is $-(\text{C}_{0-6}\text{alkyl})\text{-phenyl}$,

where the alkyl is unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from:

10

- (a) halo,
- (b) hydroxy,
- (c) $-\text{O}-\text{C}_{1-3}\text{alkyl}$, and
- (d) trifluoromethyl,

and where the phenyl is unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from:

15

- (a) halo,
- (b) trifluoromethyl,
- (c) hydroxy,
- (d) $\text{C}_{1-3}\text{alkyl}$,
- (e) $-\text{O}-\text{C}_{1-3}\text{alkyl}$,
- (f) $-\text{CO}_2\text{R}^9$,
- (g) $-\text{CN}$,
- (h) $-\text{NR}^9\text{R}^{10}$, and
- (i) $-\text{CONR}^9\text{R}^{10}$;

20

25 R^4 is selected from:

- (a) hydrogen,
- (b) hydroxy,
- (c) $\text{C}_{1-6}\text{alkyl}$,
- (d) $\text{C}_{1-6}\text{alkyl-hydroxy}$,
- (e) $-\text{O}-\text{C}_{1-3}\text{alkyl}$,
- (f) $-\text{CO}_2\text{R}^9$,
- (g) $-\text{CONR}^9\text{R}^{10}$, and
- (h) $-\text{CN}$;

30

or where R³ and R⁴ may be joined together to form a ring which is selected from:

- (a) 1H-indene,
- (b) 2,3-dihydro-1H-indene,
- (c) 2,3-dihydro-benzofuran,
- (d) 1,3-dihydro-isobenzofuran,
- (e) 2,3-dihydro-benzothiofuran, and
- (f) 1,3-dihydro-isobenzothiofuran,

or where R³ and R⁵ or R⁴ and R⁶ may be joined together to form a ring which is phenyl,

wherein the ring is unsubstituted or substituted with 1-7 substituents where the

substituents are independently selected from:

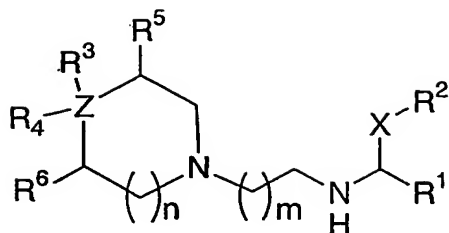
- (a) halo,
- (b) trifluoromethyl,
- (c) hydroxy,
- (d) C₁₋₃alkyl,
- (e) -O-C₁₋₃alkyl,
- (f) -CO₂R⁹,
- (g) -CN,
- (h) -NR⁹R¹⁰, and
- (i) -CONR⁹R¹⁰;

R⁵ and R⁶ are independently selected from:

- (a) hydrogen,
- (b) hydroxy,
- (c) C₁₋₆alkyl,
- (d) C₁₋₆alkyl-hydroxy,
- (e) -O-C₁₋₃alkyl,
- (f) oxo, and
- (g) halo;

and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

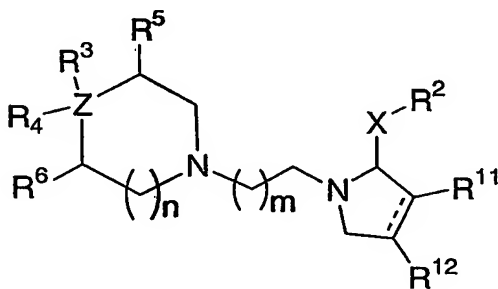
2. The compound of Claim 1 of the formula Ia:



Ia

and pharmaceutically acceptable salts and individual diastereomers thereof.

5 3. The compound of Claim 1 of the formula Ib:

**Ib**

10 wherein:
the dashed line represents a single or a double bond;

R^{11} is selected from:

- | | | |
|----|-----|--|
| 15 | (a) | hydrogen |
| | (b) | C ₁₋₆ alkyl |
| | (c) | hydroxy, |
| | (d) | -O-C ₁₋₃ alkyl |
| | (e) | -Phenyl and heterocycle, |
| | (f) | -CO ₂ R ⁹ , |
| 20 | (g) | -CN, |
| | (h) | -NR ⁹ R ¹⁰ , and |
| | (i) | -CONR ⁹ R ¹⁰ ; |

R^{12} is selected from:

- (a) hydrogen,
- (b) hydroxy,
- (c) C₁₋₆alkyl,
- (d) C₁₋₆alkyl-hydroxy,
- (e) -O-C₁₋₃alkyl,
- (f) -CO₂R⁹,
- (g) -CONR⁹R¹⁰, and
- (h) -CN;

10 or where R¹¹ and R¹² may be joined together to form a ring which is selected from:

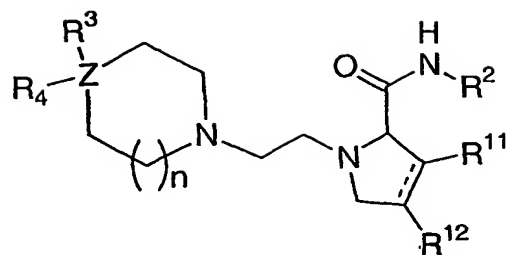
- (a) benzene,
- (b) furan,
- (c) thiophene,
- (d) thiazole,
- (e) C₃₋₆cycloalkyl

15 wherein the ring is unsubstituted or substituted with 1-7 substituents where the substituents are independently selected from:

- (a) halo,
- (b) trifluoromethyl,
- (c) hydroxy,
- (d) C₁₋₃alkyl,
- (e) -O-C₁₋₃alkyl,
- (f) -CO₂R⁹,
- (g) -CN,
- (h) -NR⁹R¹⁰, and
- (i) -CONR⁹R¹⁰;

and pharmaceutically acceptable salts and individual diastereomers thereof.

30 4. The compound of Claim 3 of the formula Id:

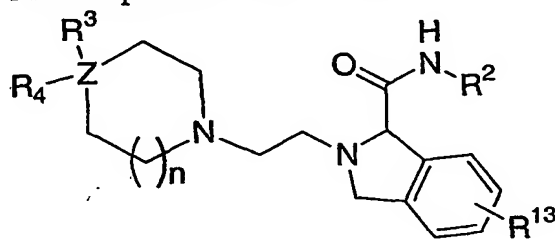


Id

and pharmaceutically acceptable salts and individual diastereomers thereof.

5

5. The compound of Claim 3 of the formula Ie:



Ie

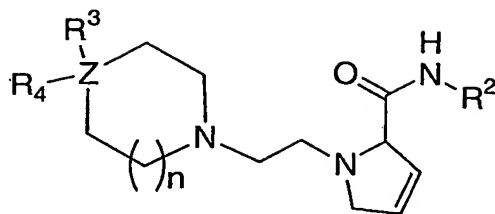
wherein R¹³ is independently selected from:

- 10 (a) hydrogen,
 (b) halo,
 (c) trifluoromethyl,
 (d) fused C₁₋₃cycloalkyl
 (e) C₁₋₃alkyl,
 15 (f) -O-C₁₋₃alkyl,
 (g) -CO₂H,
 (h) -CO₂C₁₋₃alkyl, and
 (i) -CN;

and pharmaceutically acceptable salts and individual diastereomers thereof.

20

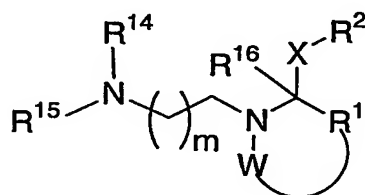
6. The compound of Claim 3 of the formula If:



If

and pharmaceutically acceptable salts and individual diastereomers thereof.

7. The compound of Claim 1 of the formula II:



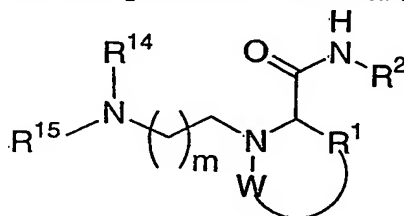
II

wherein R¹⁴, R¹⁵, R¹⁶ are independently selected from:

- (a) hydrogen,
- (b) -C₁-6alkyl
- (c) -C₁-6cycloalkyl
- (d) -C₁-6alkyl-phenyl
- (e) -C₁-6alkyl-heterocycle
- (f) -C₁-6alkyl-C₃-6cycloalkyl
- (g) -C₁-6alkyl O-C₁-6alkyl,

and pharmaceutically acceptable salts and individual diastereomers thereof.

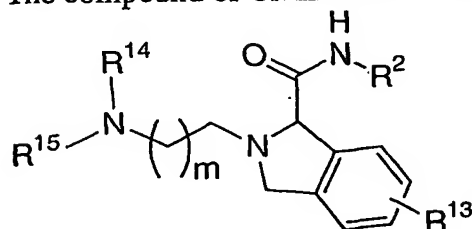
8. The compound of Claim 1 of the formula IIa:



IIa

and pharmaceutically acceptable salts and individual diastereomers thereof.

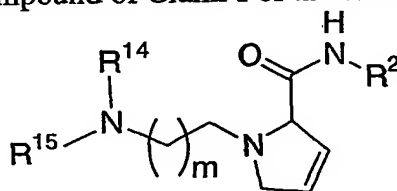
9. The compound of Claim 1 of the formula IIb:



IIb

and pharmaceutically acceptable salts and individual diastereomers thereof.

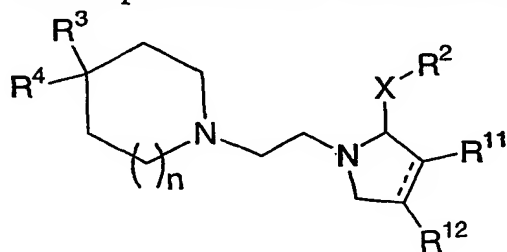
10. The compound of Claim 1 of the formula IIc:



IIc

and pharmaceutically acceptable salts and individual diastereomers thereof.

11. The compound of Claim 1 of the formula:



wherein:

the dashed line represents a single or a double bond,

R¹¹ and R¹² are hydrogen or where R¹¹ and R¹² may be joined together to form a ring which is selected from:

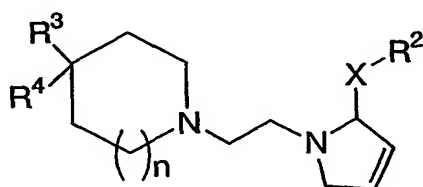
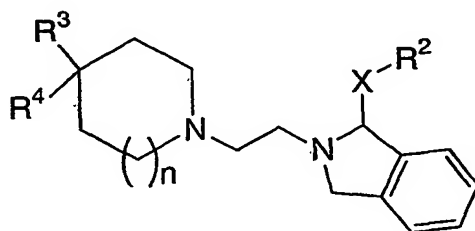
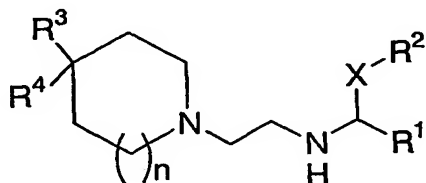
(a) benzene,

(b) heterocycle

(c) C3-6cycloalkyl

and pharmaceutically acceptable salts and individual diastereomers thereof.

5 12. The compound of Claim 1 of the formula:



and pharmaceutically acceptable salts and individual diastereomers thereof.

- 10 13. The compound of Claim 1 wherein W is hydrogen or
-CH₂-.
- 15 14. The compound of Claim 1 wherein X is -CONH-, phenyl or heterocycle.
- 15 15. The compound of Claim 1 wherein Z is -C- or -N-.
16. The compound of Claim 1 wherein n is 0 and 1.

17. The compound of Claim 1 wherein m is 1.

18. The compound of Claim 1 wherein heterocycle is selected from: furanyl, imidazolyl, oxadiazolyl, oxazolyl, pyrazolyl, pyrazinyl, pyridyl, pyridazinyl, pyrimidyl, pyrrolyl, thiadiazolyl, thiazolyl, thienyl, and triazolyl, and N-oxides thereof.

19. The compound of Claim 1 wherein -C₁₋₆alkyl, -C₀₋₆alkyl-O-C₁₋₆alkyl-, -C₀₋₆alkyl-S-C₁₋₆alkyl-, and -(C₀₋₆alkyl)-(C₃₋₇cycloalkyl)-(C₀₋₆alkyl), where the alkyl and the cycloalkyl are unsubstituted or substituted with 1-7 substituents where the substituents are independently selected from:

- (a) halo,
- (b) hydroxy,
- (c) -O-C₁₋₃alkyl,
- (d) trifluoromethyl,
- (f) C₁₋₃alkyl,
- (g) -O-C₁₋₃alkyl,
- (h) -CO₂R⁹, wherein R⁹ is independently selected from: hydrogen, C₁₋₆alkyl, C₅₋₆ cycloalkyl, benzyl or phenyl, which is unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from: halo, C₁₋₃alkyl, C₁₋₃alkoxy and trifluoromethyl,
- (i) -CN,
- (j) -NR⁹R¹⁰, and
- (k) -CONR⁹R¹⁰.

20. The compound of Claim 1 wherein R¹ is selected from:

- (1) -C₁₋₆alkyl, which is unsubstituted or substituted with 1-6 substituents where the substituents are independently selected from:
 - (a) halo,
 - (b) hydroxy,
 - (c) -O-C₁₋₃alkyl, and
 - (d) trifluoromethyl,
- (2) -C₀₋₆alkyl-O-C₁₋₆alkyl-, which is unsubstituted or substituted with 1-6 substituents where the substituents are independently selected from:

- (a) halo, and
(b) trifluoromethyl,
(3) -C₀₋₆alkyl-S-C₁₋₆alkyl-, which is unsubstituted or substituted with 1-6
substituents where the substituents are independently selected from:
5 (a) halo, and
(b) trifluoromethyl,
(4) -(C₃₋₅cycloalkyl)-(C₀₋₆alkyl), which is unsubstituted or substituted with 1-7
substituents where the substituents are independently selected from:
(a) halo,
10 (b) hydroxy,
(c) -O-C₁₋₃alkyl, and
(d) trifluoromethyl.

21. The compound of Claim 1 wherein R¹ is selected from:

- 15 (1) -CH₃,
(2) -CH₂CH₃,
(3) -CH(CH₃)₂,
(4) -CH₂CH₂CH₃,
(5) -CH₂CH(CH₃)₂,
20 (6) -cyclopropyl,
(7) -cyclobutyl,
(8) -cyclopentyl,
(9) -CH₂-cyclopropyl,
(10) -CH₂-cyclobutyl,
25 (11) -CH₂-cyclopentyl,
(12) -CH₂OH,
(13) -C(CH₃)₂(OH),
(14) -C(CH₂OH)(CH₃)₂,
(15) -(OH)cyclobutyl,
30 (16) -(OH)cyclopentyl,
(17) -C(CH₃)₂(NHCOCH₃),
(18) -C(CO₂H)(CH₃)₂,
(19) -O-CH₃,
(20) -O-cyclopentyl,

- (21) -O-CH(CH₃)₂,
- (22) -S-CH₃,
- (23) -S-CF₃,
- (24) -SO₂-CH₃,
- 5 (25) -S-CH(CH₃)₂,
- (26) -SO₂-CH(CH₃)₂, and
- (27) -NH-SO₂-CH₃.

22. The compound of Claim 1 wherein R² is selected from
 10 -(C₀₋₄alkyl)-phenyl and -(C₀₋₄alkyl)-heterocycle,
 where heterocycle is selected from:
 furanyl, imidazolyl, oxadiazolyl, oxazolyl, pyrazolyl, pyrazinyl, pyridyl,
 pyridazinyl, pyrimidyl, pyrrolyl, thiadiazolyl, thiazolyl, thienyl, and triazolyl, and
 N-oxides thereof,
 15 where the alkyl is unsubstituted or substituted with 1-7 substituents where the
 substituents are independently selected from:
 (a) halo,
 (b) hydroxy,
 (c) -O-C₁₋₃alkyl, and
 20 (d) trifluoromethyl,
 and where the phenyl or heterocycle is unsubstituted or substituted with 1-5 substituents
 where the substituents are independently selected from:
 (a) halo,
 (b) trifluoromethyl,
 25 (c) trifluoromethoxy,
 (d) hydroxy,
 (e) C₁₋₃alkyl,
 (f) -O-C₁₋₃alkyl,
 (g) -CO₂R⁹,
 30 (h) -S-C₁₋₃alkyl,
 (i) -SO₂-C₁₋₃alkyl,
 (j) -SCF₃,
 (k) -CO₂R⁹,
 (l) -NR⁹R¹⁰,

- (m) $-\text{NR}^9\text{-SO}_2\text{-R}^{10}$,
- (n) $-\text{SO}_2\text{-NR}^9\text{R}^{10}$, and
- (o) $-\text{CONR}^9\text{R}^{10}$.

5 23. The compound of Claim 1 wherein R^2 is selected from
-(C₀₋₄alkyl)-phenyl and -(C₀₋₄alkyl)-heterocycle,

where heterocycle is selected from: pyridyl, pyridazinyl, and N-oxides thereof,

where the alkyl is unsubstituted or substituted with 1-7 substituents where the
substituents are independently selected from:

- 10 (a) halo,
 (b) hydroxy,
 (c) $-\text{O-C}_{1-3}\text{alkyl}$, and
 (d) trifluoromethyl,

and where the phenyl or heterocycle is unsubstituted or substituted with 1-3 substituents

15 where the substituents are independently selected from:

- (a) halo,
 (b) trifluoromethyl,
 (c) trifluoromethoxy,
 (d) hydroxy,
20 (e) $\text{C}_{1-3}\text{alkyl}$,
 (f) $-\text{O-C}_{1-3}\text{alkyl}$,
 (g) $-\text{CO}_2\text{-C}_{1-3}\text{alkyl}$,
 (h) $-\text{CO}_2\text{H}$,
 (i) $-\text{S-C}_{1-3}\text{alkyl}$,
25 (j) $-\text{SO}_2\text{-C}_{1-3}\text{alkyl}$,
 (k) $-\text{SCF}_3$,
 (l) $-\text{NH}_2$,
 (m) $-\text{NH-SO}_2\text{-C}_{1-3}\text{alkyl}$, and
 (n) $-\text{SO}_2\text{-NH}_2$.

30 24. The compound of Claim 1 wherein R^2 is selected from $-\text{CH}_2\text{-phenyl}$ and -
 $\text{CH}_2\text{-heterocycle}$,

where heterocycle is selected from: pyridyl, pyridazinyl, and N-oxides thereof,

and where the phenyl or heterocycle is unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from:

- (a) halo,
- (b) trifluoromethyl,
- (c) trifluoromethoxy,
- (d) hydroxy,
- (e) C₁₋₃alkyl,
- (f) -O-C₁₋₃alkyl,
- (g) -CO₂-C₁₋₃alkyl,
- (h) -CO₂H,
- (i) -S-C₁₋₃alkyl,
- (j) -SO₂-C₁₋₃alkyl,
- (k) -SCF₃,
- (l) -NH₂,
- (m) -NH-SO₂-C₁₋₃alkyl, and
- (n) -SO₂-NH₂.

25. The compound of Claim 1 wherein R² is selected from:

- (1) -CH₂-(phenyl),
- (2) -CH₂-(4-bromophenyl),
- (3) -CH₂-(3-chlorophenyl),
- (4) -CH₂-(3,5-difluorophenyl),
- (5) -CH₂-((2-trifluoromethyl)phenyl),
- (6) -CH₂-((3-trifluoromethyl)phenyl),
- (7) -CH₂-((4-trifluoromethyl)phenyl),
- (8) -CH₂-((3-trifluoromethoxy)phenyl),
- (9) -CH₂-((3-trifluoromethylthio)phenyl),
- (10) -CH₂-((3-trifluoromethoxy-5-thiomethyl)phenyl),
- (11) -CH₂-((3-trifluoromethoxy-5-methoxy)phenyl),
- (12) -CH₂-((3-trifluoromethoxy-5-methanesulfonyl)phenyl),
- (13) -CH₂-((3-trifluoromethoxy-5-amino)phenyl),
- (14) -CH₂-((3-trifluoromethoxy-5-aminomethanesulfonyl)phenyl),
- (15) -CH₂-((3-trifluoromethoxy-5-sulfonylamino)phenyl),
- (16) -CH₂-((3,5-bis-trifluoromethyl)phenyl),

- (17) $-\text{CH}_2-((3\text{-fluoro-5-trifluoromethyl})\text{phenyl})$,
(18) $-\text{CH}(\text{CH}_3)-((3,5\text{-bis-trifluoromethyl})\text{phenyl})$,
(19) $-\text{C}(\text{CH}_3)_2-((3,5\text{-bis-trifluoromethyl})\text{phenyl})$,
(20) $-\text{CH}_2-(4-(2\text{-trifluoromethyl})\text{pyridyl})$,
5 (21) $-\text{CH}_2-(5-(3\text{-trifluoromethyl})\text{pyridyl})$,
(22) $-\text{CH}_2-(5-(3\text{-trifluoromethyl})\text{pyridazinyl})$,
(23) $-\text{CH}_2-(4-(2\text{-trifluoromethyl})\text{pyridyl-N-oxide})$, and
(24) $-\text{CH}_2-(5-(3\text{-trifluoromethyl})\text{pyridyl-N-oxide})$.

10 26. The compound of Claim 1 wherein R^3 is hydrogen and phenyl, where the phenyl is unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from:

- (a) halo,
(b) trifluoromethyl,
15 (c) hydroxy,
(d) $\text{C}_1\text{-3alkyl}$,
(e) $-\text{O}-\text{C}_1\text{-3alkyl}$,
(f) $-\text{CO}_2\text{R}^9$,
(g) $-\text{CN}$,
20 (h) $-\text{NR}^9\text{R}^{10}$, and
(i) $-\text{CONR}^9\text{R}^{10}$.

25 27. The compound of Claim 1 wherein R^3 is hydrogen and phenyl, where the phenyl is unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from:

- (a) halo,
(c) hydroxy,
(d) $\text{C}_1\text{-3alkyl}$,
(e) $-\text{O}-\text{C}_1\text{-3alkyl}$, and
30 (f) $-\text{CO}_2\text{R}^9$.

28. The compound of Claim 1 wherein R^3 is phenyl, or para-fluorophenyl.

29. The compound of Claim 1 wherein R⁴ is selected from:

- (a) hydrogen,
- (b) hydroxy,
- (c) -CO₂H,
- (d) -CO₂C₁₋₆alkyl, and
- (e) -CN.

30. The compound of Claim 1 wherein R⁵ and R⁶ are independently selected from:

- (a) hydrogen,
- (b) hydroxy,
- (c) -CH₃,
- (d) -O-CH₃, and
- (e) oxo.

31. A compound which is selected from the group consisting of the title compounds of the Examples, and pharmaceutically acceptable salts and individual diastereomers thereof.

32. A pharmaceutical composition which comprises an inert carrier and a compound of Claim 1.

33. A method for modulation of chemokine receptor activity in a mammal in need thereof which comprises the administration of an effective amount of the compound of Claim 1.

34. A method for treating, ameliorating or controlling an inflammatory or immunoregulatory disorder or disease which comprises administering to a patient in need thereof an effective amount of the compound of Claim 1.

35. A method for reducing the risk of an inflammatory or immunoregulatory disorder or disease which comprises administering to a patient in need thereof an effective amount of the compound of Claim 1.

36. A method for treating, ameliorating or controlling rheumatoid arthritis which comprises administering to a patient in need thereof an effective amount of the compound of Claim 1.